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April 15, 2003

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Re: Appellants: Timothy P. Tully *et al.*
Application No.: 09/523,066 Filed: March 10, 2000
Confirmation No.: 4462
Title: GENE CHIP TECHNOLOGY FOR DETERMINING MEMORY GENES
Docket No.: 1314.1058-001

Sir:

Transmitted herewith are three (3) originally signed copies of a Brief on Appeal for filing in the subject application. The Brief on Appeal is filed pursuant to the Notice of Appeal received by the U.S. Patent and Trademark Office on October 15, 2002.

1. [X] Appellant hereby petitions to extend the time for filing a Brief on Appeal for four months from December 15, 2002 to April 15, 2003.

2. [ ] A [ ] month extension of time to extend the time for filing a Brief on Appeal from [ ] to [ ] was filed on [ ] with payment of a $[ ] fee.

[ ] Appellant hereby petitions for an additional [ ] month extension of time for filing a Brief on Appeal from [ ] to [ ].

3. [ ] A Request for Oral Hearing before the Board of Patent Appeals and Interferences is being filed concurrently herewith.

4. Fees are submitted for the following:

[X]	Extension of Time for three months		$ 1450
[ ]	Additional Extension of Time:		
	Fee for Extension ([ ] mo.)	$	
	Less fee paid ([ ] mo.)	- $	
	Balance of fee due		$ 0
[X]	Brief on Appeal		$ 320
[ ]	Other		$
		TOTAL	$ 1770

5. The method of payment for the total fees is as follows:

[X] A check in the amount of $1770.00 is enclosed.

[ ] Please charge Deposit Account No. 08-0380 in the amount of $[ ].

Please charge any deficiency or credit any overpayment in the fees that may be due in this matter to Deposit Account No. 08-0380. A copy of this letter is enclosed for accounting purposes.

Respectfully submitted,

HAMILTON, BROOK, SMITH & REYNOLDS, P.C.

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Dated: April 15, 2003

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE
BEFORE THE BOARD OF PATENT APPEALS AND INTERFERENCE

Appellants: Timothy P. Tully, Joshua I. Dubnau, Michael Davis, Jan Mous and Ulrich Certa

Application No.: 09/523,066 Group Art Unit: 1634

Filed: March 10, 2000 Examiner: B. Forman

Confirmation No.: 4462

For: GENE CHIP TECHNOLOGY FOR DETERMINING MEMORY GENES

CERTIFICATE OF MAILING
I hereby certify that this correspondence is being deposited with the United States Postal Service with sufficient postage as First Class Mail in an envelope addressed to Assistant Commissioner for Patents, P.O. Box 2327, Arlington, VA 22202
on 4-15-03 Laura M Myers
Date Signature
Laura M Myers
Typed or printed name of person signing certificate

BRIEF ON APPEAL

Box AF
Assistant Commissioner for Patents
P.O. Box 2327
Arlington, VA 22202

Sir:

This Brief on Appeal is submitted pursuant to the Notice of Appeal received in the U.S. Patent and Trademark Office on October 15, 2002, and in support of the appeal from the final rejections set forth in the Office Action mailed on April 10, 2002 (Paper No. 14). The fee for

filing a brief in support of an appeal is enclosed. A Petition for Extension of Time and the appropriate fee are being filed concurrently.

I. REAL PARTY IN INTEREST

The real parties in interest are Cold Spring Harbor Laboratory, One Bungtown Road, Cold Spring Harbor, New York 11724; Emory University, 1380 South Oxford Road, N.E., Atlanta, Georgia 30322; Hoffmann-La Roche Inc., 340 Kingsland Street, Nutley, New Jersey 07110; and Helicon Therapeutics, Inc., One Bioscience Park Drive, Farmingdale, New York 11735. Cold Spring Harbor Laboratory, Emory University and Hoffmann-La Roche Inc. are the Assignees of the entire right, title and interest in the subject application. Cold Spring Harbor Laboratory is an Assignee pursuant to an Assignment recorded on April 17, 2000 at Reel 010772, Frames 0345-0351. Emory University is an Assignee pursuant to an Assignment recorded on April 17, 2000 at Reel 010772, Frames 0302-0304. Hoffmann-La Roche Inc. is an Assignee pursuant to an Assignment recorded on May 1, 2000 at Reel 010790, Frames 0641-0642. Helicon Therapeutics, Inc. is the licensee of the subject matter described in the subject application.

II. RELATED APPEALS AND INTERFERENCES

Appellants, the undersigned Attorney, Assignees and Licensee are not aware of any related appeals or interferences which will directly affect or be directly affected by or have a bearing on the Board's decision in the pending appeal.

III. STATUS OF CLAIMS

As filed, the instant application contained Claims 1-26. Pursuant to the restriction requirement set forth in the Office Action dated November 20, 2000 (Paper No. 7), Appellants elected to prosecute the invention of Group II (Claims 11-15 and 24-26). Claims 1-10 and 16-23 were withdrawn from further consideration by the Examiner as being drawn to a non-elected invention. Claim 14 was cancelled in Amendment B filed on January 14, 2002. Thus, Claim 11-13, 15 and 24-26 are pending and subject to this appeal. The pending claims, as they stood upon final rejection, are presented in the Appendix of this Brief. Claims 11, 15 and 24

were amended in Amendment A filed on May 21, 2001 and/or Amendment B filed on January 14, 2002. Claims 12, 13, 25 and 26 appear as originally filed.

IV. STATUS OF AMENDMENTS

No Amendments have been filed subsequent to the mailing of the Office Action dated April 10, 2002 (Paper No. 14).

A Petition under 37 C.F.R. § 1.144 was filed on January 14, 2002 and has not been considered by the Patent Office. The Petition was filed to obtain review of the Examiner's decision to maintain the restriction requirement.

V. SUMMARY OF INVENTION

The claimed invention relates to methods of identifying a gene or genes involved in transcription-dependent memory in Drosophila comprising training Drosophila to induce transcription-dependent memory formation in the Drosophila; extracting RNA from head tissue of the trained Drosophila; synthesizing labeled cDNA probes complementary to the extracted RNA; hybridizing the synthesized DNA probes to microarray chips containing DNA sequences from genes of the Drosophila genome under conditions appropriate for hybridization of the DNA probes to complementary DNA sequences on the microarray chips, wherein a signal is produced upon hybridization of the probes to complementary DNA sequences; detecting the signal produced; and performing a statistical comparison between the detected signal and the signal detected in a control (Claims 11-13, 15 and 24-26). In some embodiments of the invention, control Drosophila are trained under conditions insufficient to induce transcription-dependent memory formation (Claims 11-13 and 15), but sufficient to induce transcription-independent memory formation (Claim 15). In other embodiments of the invention, control Drosophila are naïve (untrained) flies (Claims 24-26). In a particular embodiment of the invention, transcription-dependent memory formation is long term memory formation (Claims 12 and 25). In some embodiments of the invention, transcription-dependent memory formation is induced using a spaced training protocol (Claims 13 and 26) and transcription-independent memory formation is induced using a massed training protocol (Claim 15).

VI. ISSUE

The sole issue on appeal is whether Claims 11-15 and 24-26 are properly rejected under 35 U.S.C. § 103(a) as being obvious over Yin *et al.* (*Cell*, 79:49-58 (1994)) in view of Ramsey (*Nature Biotechnology*, 16:40-44 (1998)) and Tully *et al.* (U.S. Patent No. 5,929,223).

VII. GROUPING OF CLAIMS

With respect to the sole issue, Claims 11-13, 15 and 24-26 stand or fall together.

VIII. ARGUMENT

Claims 11-15 and 24-26 are rejected under 35 U.S.C. § 103(a) as being obvious over Yin *et al.* (*Cell*, 79:49-58 (1994)) in view of Ramsey (*Nature Biotechnology*, 16:40-44 (1998)) and Tully *et al.* (U.S. Patent No. 5,929,223). Paper No. 14, at page 3, lines 3-5. Since Claim 14 was cancelled in Amendment B, it is assumed that the rejection does not apply to the cancelled claim.

Teachings of the Cited References

Yin *et al.*

Yin *et al.* teach the use of a dominant negative CREB transgene to investigate the role of CREB in long term memory (LTM) formation in Drosophila. In particular, Yin *et al.* teach the use of the inducible transgene approach in combination with training protocols for inducing memory formation to investigate the effect of inducing a dominant negative CREB transgene on LTM formation. More specifically, Yin *et al.* teach the production of transgenic flies that express *dCREB2-b* under the control of a heat-shock promoter (*hs-dCREB2-b* transgene), training the transgenic flies which had been heat-shock induced or left uninduced, under conditions appropriate to induce memory formation in the flies, extracting RNA from the head tissue of trained flies, exposing the extracted RNA to a dCREB2-b cDNA fragment under conditions appropriate for hybridization of dCREB2-b transgene RNA to the dCREB2-b cDNA fragment and detecting hybridization of dCREB2-b transgene RNA to the dCREB2-b cDNA fragment. The hybridization signal detected using RNA extracted from the heads of trained transgenic flies is compared to the hybridization signal detected using RNA extracted from the

heads of wildtype flies (i.e., flies that do not include the *hs-dCREB2-b* transgene) trained in the same manner as the transgenic flies (Yin *et al.*, page 50, Figure 1A).

Yin *et al.* also disclose the results of behavioral experiments in which the performance index of the trained flies is measured (Yin *et al.*, page 51, column 2 to page 53, column 2) and provide particular methods for statistically analyzing the behavioral data obtained for the CREB transgene (Yin *et al.*, page 55, column 2, second paragraph from bottom ("Statistical Analyses of Behavioral Data") to page 56, column 2, fourth full paragraph ("Shock Reactivity in rsh;17-2 Flies (Table 1)").

Thus, Yin *et al.* simply demonstrate that functional regulation of CREB itself is both necessary and sufficient for modulation of long-term memory formation (LTM). Downregulation of CREB leads to suppression of LTM. Upregulation of CREB leads to enhancement of LTM.

Yin *et al.* do not teach or suggest the use of microarray chips in a method to identify genes involved in transcription-dependent memory formation. Also, Yin *et al.* do not teach or suggest the use of a statistical comparison between signal detected from a control microarray chip and signal detected on a microarray chip using cDNA probes synthesized from RNA extracted from head tissue of Drosophila trained under conditions appropriate to induce transcription-dependent memory to identify genes involved in transcription-dependent memory formation.

The Declaration of Timothy P. Tully, Ph.D. under 37 C.F.R. § 1.132 filed concurrently herewith supports Appellants' assessment of the teachings of the Yin *et al.* reference.

Tully *et al.*

Tully *et al.* is cited by the Examiner as teaching "the method wherein the hybridization signals from the spaced trained and massed trained Drosophila are compared." In particular, the Examiner contends that in column 25, lines 6-30, Tully *et al.* teach:

> training two groups of Drosophila, one under conditions to induce transcription-dependent memory and a second under condition insufficient to induce transcription-dependent memory, extracting RNA from head tissue of both groups, hybridizing the RNA to DNA sequences from genes of the Drosophila and comparing the hybridization signals between the two groups.

Paper No. 10, at page 7, lines 6-11. Respectfully, it appears that the Examiner may have misunderstood the cited passage. It is noted that Example 2, which includes column 25, lines 6-30, is the same as or similar to the "Experimental Procedures" (pages 55 to 57) and "Results" (pages 50 to 53) sections of the Yin *et al.* reference.

At column 25, lines 6-30, Tully *et al.* disclose the method for performing Northern analysis, which is the same as or similar to the method disclosed by Yin *et al.* (see Yin *et al.*, at page 56, column 2, last paragraph). At column 26, lines 9-15, Tully *et al.* report the results revealed by Northern analysis, which are the same as or similar to the results reported by Yin *et al.* (see Yin *et al.*, at page 50, column 2, last paragraph).

Similarly, in Example 2, Tully *et al.* teach the use of a dominant negative CREB transgene to investigate the role of CREB in LTM formation in Drosophila. In particular, Tully *et al.* teach the use of the inducible transgene approach in combination with training protocols for inducing memory formation to investigate the effect of inducing a dominant negative CREB transgene on LTM formation. More specifically, Tully *et al.* teach the production of transgenic flies that express *dCREB2-b* under the control of a heat-shock promoter (*hs-dCREB2-b* transgene), training the transgenic flies which had been heat-shock induced or left uninduced, under conditions appropriate to induce memory formation in the flies, extracting RNA from the head tissue of trained flies, exposing the extracted RNA to a dCREB2-b cDNA fragment under conditions appropriate for hybridization of dCREB2-b transgene RNA to the dCREB2-b cDNA fragment and detecting hybridization of dCREB2-b transgene RNA to the dCREB2-b cDNA fragment. The hybridization signal detected using RNA extracted from the heads of trained transgenic flies is compared to the hybridization signal detected using RNA extracted from the heads of wildtype flies (i.e., flies that do not include the *hs-dCREB2-b* transgene) trained in the same manner as the transgenic flies (Tully *et al.*, column 3, lines 36-41; and Figure 9A).

In Example 2, Tully *et al.* also disclose the results of behavioral experiments in which the performance index of the trained flies is measured (Tully *et al.*, column 26, line 52 to column 28, line 41) and provide particular methods for statistically analyzing the behavioral data obtained for the CREB transgene (Tully *et al.*, column 23, line 1 to column 25, line 5).

Thus, Tully *et al.* simply demonstrate that functional regulation of CREB itself is both necessary and sufficient for modulation of long-term memory formation (LTM). Downregulation

of CREB leads to suppression of LTM. Upregulation of CREB leads to enhancement of LTM. Tully *et al.* also disclose drug or gene manipulations to accomplish this modulation of CREB and the corresponding enhancement/suppression of long-term memory formation.

Tully *et al.* do not teach or suggest the use of microarray chips in a method to identify genes involved in transcription-dependent memory formation. Also, Tully *et al.* do not teach or suggest the use of a statistical comparison between signal detected from a control microarray chip and signal detected on a microarray chip using cDNA probes synthesized from RNA extracted from head tissue of Drosophila trained under conditions appropriate to induce transcription-dependent memory to identify genes involved in transcription-dependent memory formation.

The Rule 132 Declaration of Dr. Tully filed concurrently herewith supports Appellants' assessment of the teachings of the Tully *et al.* patent.

Ramsey

Ramsey is a 1998 review article describing the state of the art of DNA chip technology, including its successful application "to the simultaneous expression of many thousands of genes and to large-scale gene discovery" (Ramsey, page 40, abstract). For example, Ramsey reports the successful use of DNA arrays to measure differential gene expression in plants, yeast and human samples (Ramsey, page 41, column 1). Thus, Ramsey describes a general method to detect transcriptionally regulated genes using DNA microarray techniques.

Ramsey does not teach or suggest performing a gene chip identification of those genes expressed during transcription-dependent memory formation but not during transcription-independent memory formation. Importantly, Ramsey does not describe in detail any statistical method for the selection of significant treatment effects from such microarray data, and he does not describe any method to identify any subset of genes, which are transcriptionally regulated during long-term memory formation.

The Rule 132 Declaration of Dr. Tully filed concurrently herewith supports Appellants' assessment of the teachings of the Ramsey reference.

The Combination of References

In support of the rejection, the Examiner alleges that it would have been prima facie obvious "to modify the northern blot gene identification of Yin *et al.* with the microarray identification exhibiting 10 fold sensitivity when compared to Northern Blots as taught by Ramsey wherein multiple response-specific genes are identified for the expected benefit of large-scale, rapid identification of expression-specific genes as taught by Ramsey" (Paper No. 14, at page 4, lines 13-17; page 6, lines 19-23; page 7, lines 17-21; and page 8, lines 27-33) and "to modify the RNA analysis of Yin *et al.* wherein hybridization signals from trained and untrained Drosophila are compared to further compare hybridization signals from Drosophila following the different training protocols as taught by Tully *et al.* for the obvious benefit of analyzing training-specific expression to thereby identify memory-specific expression" (Paper No. 14, at page 5, lines 6-9).

Appellants respectfully submit that this rejection is improper because the Examiner has not identified a suggestion in the prior art of the desirability of the proposed combination of references. Combining the elements of separate references which do not themselves suggest the combination necessary to obtain a claimed invention is generally improper. ACS Hospital Systems, Inc. v. Montefiore Hospital, 221 U.S.P.Q. 929, 933 (Fed. Cir. 1984). The only document of record which suggests the desirability of the proposed combination is Appellants' specification. However, the use of the present specification as an instruction manual or template to piece together the teachings of the prior art is impermissible hindsight.

Notwithstanding the above, a *prima facie* case of obviousness is established only if the teachings of the cited art would have suggested the claimed invention to one of ordinary skill in the art with a reasonable expectation of successfully achieving the claimed results. In re Vaeck, 20 U.S.P.Q.2d 1438, 1442 (Fed. Cir. 1991). Both the suggestion and the reasonable expectation of success must be found in the prior art, not Applicants' disclosure. Id.

The Court of Appeals for the Federal Circuit has stated that "[t]he proper approach to the obviousness issue must start with the claimed invention *as a whole.*" See, e.g., Kimberley-Clark Corp. v. Johnson & Johnson Co., 223 U.S.P.Q. 603, 609 (Fed. Cir. 1984). See also Lindemann

Maschinenfabrik G.m.b.H. v. American Hoist & Derrick Co., 221 U.S.P.Q. 481, 488 (Fed. Cir. 1984). It is not proper to pick and choose among individual elements of assorted prior art references to recreate the claimed invention. Smithkline Diagnostics Inc. v. Helena Laboratories Corp., 8 U.S.P.Q.2d 1468, 1475 (Fed. Cir. 1988); Akzo N.V. v. International Trade Comm., 11 U.S.P.Q.2d 1241, 1246 (Fed. Cir. 1986).

The claimed invention pertains to methods of identifying a gene or genes involved in transcription-dependent memory in Drosophila comprising training Drosophila to induce transcription-dependent memory formation in the Drosophila; extracting RNA from head tissue of the trained Drosophila; synthesizing labeled cDNA probes complementary to the extracted RNA; hybridizing the synthesized DNA probes to microarray chips containing DNA sequences from genes of the Drosophila genome under conditions appropriate for hybridization of the DNA probes to complementary DNA sequences on the microarray chips, wherein a signal is produced upon hybridization of the probes to complementary DNA sequences; detecting the signal produced; and performing a statistical comparison between the detected signal and the signal detected in a control (Claims 11-13, 15 and 24-26). In some embodiments of the invention, control Drosophila are trained under conditions insufficient to induce transcription-dependent memory formation (Claims 11-13 and 15), but sufficient to induce transcription-independent memory formation (Claim 15). In other embodiments of the invention, control Drosophila are naïve (untrained) flies (Claims 24-26). In a particular embodiment of the invention, transcription-dependent memory formation is long term memory formation (Claims 12 and 25). In some embodiments of the invention, transcription-dependent memory formation is induced using a spaced training protocol (Claims 13 and 26) and transcription-independent memory formation is induced using a massed training protocol (Claim 15). The fact that an individual element and/or feature can be located in the prior art does not support the conclusion that the claimed invention as a whole is *prima facie* obvious.

None of the cited references, alone or in their various combinations, would have suggested the claimed invention to one of ordinary skill in the art at the time the invention was made with a reasonable expectation of success. As discussed above, Yin *et al.* and Tully *et al.* teach the use of the inducible transgene approach in combination with training protocols for

inducing memory formation to investigate the effect of inducing a dominant negative CREB transgene on long term memory formation. Yin *et al.* and Tully *et al.* simply demonstrate that functional regulation of CREB itself is both necessary and sufficient for modulation of long-term memory formation (LTM). Downregulation of CREB leads to suppression of LTM. Upregulation of CREB leads to enhancement of LTM. Tully *et al.* also disclose drug or gene manipulations to accomplish this modulation of CREB and the corresponding enhancement/suppression of long-term memory formation. Additionally, Yin *et al.* and Tully *et al.* provide the data to suggest that particular comparisons of behavioral training protocols might be used conceptionally to detect transcriptionally regulated genes specific to the long-term memory formation experimentally induced (odor-shock associations) as distinct from those transcriptionally regulated genes that might respond to other nonspecific stimuli in the animals' environment/life history. However, neither the Yin *et al.* reference nor the Tully *et al.* patent teaches or suggests the use of microarray chips in a method to identify genes involved in transcription-dependent memory formation. In addition, neither the Yin *et al.* reference nor the Tully *et al.* patent teaches or suggests performing a statistical comparison between signal detected from a control microarray chip and signal detected on a microarray chip using cDNA probes synthesized from RNA extracted from head tissue of Drosophila trained under conditions appropriate to induce transcription-dependent memory to identify genes involved in transcription-dependent memory formation. While both the Yin *et al.* reference and the Tully *et al.* patent may suggest downstream genes conceptually, neither mentions it explicitly and neither provides any explicit methods (e.g., DNA microarray techniques) to identify such genes.

Ramsey does not cure the deficiencies of either the Yin *et al.* reference or the Tully *et al.* reference. Although Ramsey teaches the use of microarray chips in a method of detecting differential expression of genes, Ramsey does not teach or suggest performing a gene chip identification of those genes expressed during transcription-dependent memory formation but not during transcription-independent memory formation to yield a set of genes that are involved in transcription-dependent memory formation. Ramsey does not describe in detail any statistical method for the selection of significant treatment effects from such microarray data, and he does

not describe any method to identify any subset of genes, which are transcriptionally regulated during long-term memory formation.

In Paper No. 14, the Examiner dismissed Appellants' arguments pertaining to the Tully *et al.* patent, maintaining that "the arguments do not address the instant rejection" since "the rejection over Tully et al of Paper No. 7 was withdrawn in the rejection of Paper No. 10" (Paper No. 14, at page 7, lines 26-31). However, at page 3, lines 3-5, the Examiner stated that "Claims 11-15 and 24-26 are rejected under 35 U.S.C. 103(a) as being obvious over Yin et al. . . . in view of Ramsey . . . *and Tully et al.*" (Paper No. 14, at page 3, lines 3-5; emphasis added). At page 4, line 26 to page 5, line 5, the Examiner provided an assessment of the teachings of Tully *et al.* and at page 5, lines 6-9, the Examiner argued that it would have been obvious "to modify the RNA analysis of Yin et al. wherein hybridization signals from trained and untrained Drosophila are compared to further compare hybridization signals from Drosophila following the different training protocols *as taught by Tully et al.* for the obvious benefit of analyzing training-specific expression to thereby identify memory-specific expression" (Paper No. 14, at page 4, line 26 to page 5, line 9; emphasis added). Accordingly, the instant rejection and the specific arguments relied upon in support of the rejection are unclear, given the Examiner's conflicting statements.

Nonetheless, the cited references (Yin *et al.*, Ramsey, Tully *et al.*), either alone or in their various combinations, would not have reasonably suggested the claimed invention to one of ordinary skill in the art, at the time the invention was made, with a reasonable expectation of success. The cited references merely indicate that isolated elements and/or features recited in the claims are known. This is insufficient to render the claimed invention *prima facie* obvious.

The Rule 132 Declaration of Dr. Tully, filed concurrently herewith, supports Appellants' arguments. Accordingly, the invention of Claims 11-13, 15 and 24-26 is nonobvious over the cited references and their combined teachings.

CONCLUSION

It is respectfully requested that the rejection be reversed and that the claims be allowed. This Brief is being filed in triplicate.

Respectfully submitted,

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Date: April 15, 2003

APPENDIX

REJECTED CLAIMS OF 09/523,066

11. A method of identifying a gene or genes involved in transcription-dependent memory comprising the steps of:

(a) training Drosophila to induce transcription-dependent memory formation in said Drosophila;

(b) extracting RNA from head tissue of Drosophila trained in step (a);

(c) synthesizing labeled cDNA probes complementary to the RNA extracted in step (b);

(d) hybridizing the DNA probes synthesized in step (c) to microarray chips containing DNA sequences from genes of the Drosophila genome under conditions appropriate for hybridization of the DNA probes to complementary DNA sequences on the microarray chips, wherein a signal is produced from said labeled probes upon hybridization of said probes to complementary DNA sequences;

(e) detecting the signal produced in step (d); and

(f) performing a statistical comparison between the signal detected in step (e) and the signal detected in a control for each gene, wherein said control is obtained according to a method comprising the steps of:

(i) training control Drosophila to induce transcription-independent memory formation but not transcription-dependent memory formation in said control Drosophila;

(ii) extracting RNA from head tissue of said control Drosophila trained in step (f)(i);

(iii) synthesizing labeled cDNA probes complementary to the RNA extracted in step (f)(ii); and

(iv) hybridizing the DNA probes synthesized in step (f)(iii) to microarray chips containing DNA sequences from genes of the Drosophila genome under conditions appropriate for hybridization of the DNA probes to complementary DNA sequences on the microarray chips, wherein a signal is produced from said labeled probes upon hybridization of said probes to complementary DNA sequences.

12. The method of Claim 11 wherein said transcription-dependent memory formation is long term memory formation.

13. The method of Claim 11 wherein transcription-dependent memory formation is induced using a spaced training protocol and the conditions of step (f)(i) are those according to a massed training protocol.

15. The method of Claim 11 wherein transcription-independent memory formation is induced using a massed training protocol.

24. A method of identifying a gene or genes involved in transcription-dependent memory comprising the steps of:

(a) training Drosophila to induce transcription-dependent memory formation in said Drosophila;

(b) extracting RNA from head tissue of Drosophila trained in step (a);

(c) synthesizing labeled cDNA probes complementary to the RNA extracted in step (b);

(d) hybridizing the DNA probes synthesized in step (c) to microarray chips containing DNA sequences from genes of the Drosophila genome, wherein a signal is produced from said labeled probes upon hybridization of said probes to complementary DNA sequences;

(e) detecting the signal produced in step (d); and

(f) performing a statistical comparison between the signal detected in step (e) and the signal detected in a control for each gene, wherein said control is obtained according to a method comprising the steps of:

(i) extracting RNA from head tissue of control Drosophila;

(ii) synthesizing labeled cDNA probes complementary to the RNA extracted in step (f)(i); and

(iii) hybridizing the DNA probes synthesized in step (f)(ii) to microarray chips containing DNA sequences from genes of the Drosophila genome, wherein a signal is produced from said probes upon hybridization of said probes to complementary DNA sequences.

25. The method of Claim 24 wherein said transcription-dependent memory formation is long term memory formation.

26. The method of Claim 24 wherein transcription-dependent memory formation is induced using a spaced training protocol.